

III. REMARKS

A. STATUS OF THE CLAIMS

Claims 1-3 and 16-20 were pending in this application. Claims 4-15 were previously cancelled. Claims 1 and 3 are amended herein.

Applicants believe that *no new subject matter* has been added to the claims by these amendments. The applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Accordingly, upon the entry of the present amendments, claims 1-3 and 16-20 will remain pending.

B. 35 U.S.C. § 112 SECOND PARAGRAPH REJECTIONS

Claim 3 was rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicant respectfully traverses this rejection.

The Office Action mailed September 11, 2007, at page 3, contends that "it is not clear how the sequence product (with attached dye labels) can be subjected to further sequencing reaction." Without acquiescing to the validity of this rejection, and solely in an effort to expedite prosecution and allowance of the pending claims, claims 1 and 3 have been amended as follows:

Claim 1 was amended by inserting the expression "by removing unincorporated dye terminators from the sequencing reaction product". Support for this amendment, as well as the amendment to claim 3, is found at least, in the specification on page 3, lines 3-8, and Abstract, as originally filed.

Claim 3 was amended by inserting the phrase "sequencing reaction" between the terms resuspended and product.

Applicants respectfully contend that claims 1-3 and 16-20 meet the specific requirements of 35 U.S.C. § 112, second paragraph, and overcome this rejection. Applicants respectfully request that this rejection be withdrawn.

C. 35 U.S.C. § 103(a) SECOND PARAGRAPH OBVIOUSNESS REJECTIONS

1. Claims 1-3 and 17 were rejected under 35 USC 103(a), as being obvious over WO 01/19482 to *Leonard* (hereinafter referred to as "*Leonard*") in view of WO 02/44414 to *Bjerke et al.* (hereinafter referred to as "*Bjerke*").

The Office Action of September 11, 2007 admits that *Leonard* fails to teach a guanidine solution for removing unincorporated dye terminators from a sequencing reaction product as recited in claims 1 and 17. However, the Office Action appears to rely on *Bjerke* to overcome this deficiency by alleging that *Bjerke* teaches purification of DNA sequencing products having dye terminators using magnetic particles and chaotropic agents such as guanidine solutions, and that it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to use a chaotropic agent, such as a guanidine solution, for the purification of DNA. The Office Action further alleges "that a person of ordinary skill in the art would have been motivated at the time the invention was made to use a chaotropic agent, such as guanidine, for purification of DNA such as sequencing reaction products because chaotropic agents such as guanidine are known in the art for DNA purification and chaotropic agents are known to enhance nucleic acid binding to solid support for purification". The Office Action further alleges, "A person of ordinary skill in the art would have reasonable expectations of success of achieving such modifications since the techniques for using various substrates (such as membranes) for purification of DNA using chaotropic agents such as guanidine solutions are routine and known in the art as demonstrated by *Leonard* and *Bjerke*".

Applicants respectfully traverse this rejection.

The Patent and Trademark Office Action (PTO) bears the burden of initially establishing a *prima facie* case of obviousness. MPEP § 2142. The standard required to establish a *prima facie* case of obviousness comprise, "First there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine what the reference teaches. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references combined) must teach or suggest all the claim limitations." MPEP § 2143 The motivation to make the claimed invention and the reasonable expectation of success must both be found in the prior art, not the applicant's disclosure. *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir.

1991). Additionally, the references must be considered as a whole and must suggest the desirability, and thus the obviousness of making the combination.

Hodosh v. Block Drug Co., Inc., 229 U.S.P.Q. 182, 187 n.5 (Fed. Cir. 1986); MPEP § 2141.

Applicants additionally note that the Federal Circuit has repeatedly stated that “there is no basis for concluding that an invention would have been obvious solely because it is a combination of elements that were known in the art at the time of the invention. See, for example, *Smiths Industries Medical Sys., Inc v. Vital Signs Inc.*, 183 F.3d 1347, 1355, 51 U.S.P.Q.2d 1415, 1423 (Fed. Cir. 1999). The Federal Circuit also recognizes that “virtually all inventions are combinations of old elements. If identification of each claimed element in the prior art were sufficient to negate patentability, very few patents would ever issue.” See, for example, *In re Rouffet*, 149 F.3d 1350, 1356, 47 U.S.P.Q.2d 1453, 1459 (Fed. Cir. 1998)

Claim 1 is directed to a method for purifying sequencing reaction product by removing unincorporated dye terminators from a sequencing reaction, comprising:

providing sequencing reaction product;

providing at least one ultrafiltration membrane having at least one surface;

providing a solution comprising an amount of guanidine effective for removing unincorporated dye terminators from the sequencing reaction;

introducing the sequencing reaction product and the solution to at least one surface of the ultrafiltration membrane; and

applying a driving force to the ultrafiltration membrane to produce purified sequencing reaction product by removing unincorporated dye terminators from the sequencing reaction product.

In contrast, *Leonard* teaches a method for sequencing reaction cleanup adapted to remove contaminants from a sequencing reaction, comprising the steps of providing a defined quantity of sequencing reaction product, providing at least one ultrafiltration membrane having at least one surface, transferring the suspended sequencing reaction product to the surface of the ultrafiltration membrane, and applying a first constant pressure differential to the ultrafiltration membrane at a force capable of producing the sequencing reaction product substantially free of the contaminants. (page 4, lines 16-32; Abstract) Applicants respectfully contend that while *Leonard* teaches in a preferred embodiment that the sequencing reaction product is suspended in a solution of 10-15% formamide, EDTA, and water (page 6, lines 18-26), *Leonard*, as acknowledged in the Office Action, fails to teach, hint or even suggest using

guanidine to remove unincorporated dye terminators from the sequencing reaction products on a filtration membrane under pressure as instantly claimed.

Applicants respectfully contend that *Bjerke* fails to cure the deficiencies of *Leonard*. Specifically, *Bjerke* teaches methods of purifying DNA extension products from a DNA sequencing reaction containing unincorporated dideoxynucleotides, labeled primers, DNA sequencing reactions labeled with fluorescent dyes, and other materials, by using silica matrices, particularly magnetic silica particles, and an adsorption solution, configured to promote selective adsorption of DNA extension products to silica magnetic particles, leaving the labeled primers in solution. (page 9, line 14 to page 10, line 12; Abstract) The adsorption solution preferably comprises a chaotropic agent, such as guanidine hydrochloride, and a buffer, preferably having a pH of less than about 5.0. (page 12, line 31 to page 13, line 18) The concentration of guanidine is preferably at least about 1 molar up to about 7 molar. (claim 35)

While *Bjerke* teaches an adsorption solution comprising guanidine, it should be noted that *Bjerke* teaches that the guanidine adsorption solution is used with silica magnetic particles, and that the guanidine adsorption solution is specifically configured to promote selective adsorption of DNA extension products to silica magnetic particles, leaving labeled DNA sequencing reactions in solution. Applicants respectfully contend that *Bjerke* fails to teach, hint or even suggest using guanidine without the silica magnetic particles to remove unincorporated dye terminators from the sequencing reaction products on a ultrafiltration membrane while applying a driving force to the ultrafiltration membrane as instantly claimed. In addition, *Bjerke* fails to teach, hint or even suggest that using guanidine without the silica magnetic particles is capable of remove unincorporated dye terminators from the sequencing reaction products on a ultrafiltration membrane while applying a driving force to the ultrafiltration membrane as instantly claimed

Applying the aforementioned precedent to the instant case, Applicants note that each of *Leonard* and *Bjerke* fail to teach or suggest a motivation as to why one of ordinary skill in the art at the time the invention was made would combine or modify their teachings to arrive at the claimed invention. Under 35 U.S.C. 103(a), there must be some objective teaching, suggestion or motivation in the prior art that would have motivated one of ordinary skill in the art at the time the invention was made to arrive at the claimed invention as a whole. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992) Additionally, there must be a reasonable expectation of success.

Applicants contend that the combined teachings afforded by *Leonard* and *Bjerke* do not suggest Applicants' invention as claimed without using Applicants' own disclosure. *Leonard*, as the Office Action acknowledges, fails to teach, hint or suggest using guanidine to remove unincorporated dye terminators from the sequencing reaction products on a filtration membrane under pressure as instantly claimed. The Office Action appears to rely on *Bjerke* to overcome this deficiency. However, Applicants respectfully contend that *Bjerke* fails to overcome the deficiencies of *Leonard* because *Bjerke* fails teach, hint or even suggest using guanidine on a ultrafiltration membrane while applying a driving force to the ultrafiltration membrane to produce purified sequencing reaction products as instantly claimed.

Accordingly, as such, one of ordinary skill in the art would not have combined the teachings of *Leonard* with *Bjerke* or have looked to *Bjerke* as providing the motivation to modify the process of *Leonard* as alleged in the Office Action.

Furthermore, even if *arguendo*, one of ordinary skill in the art would have been motivated to combine the teachings of *Leonard* with *Bjerke*, one of ordinary skill in the art would not have arrived at the method for purifying sequencing reaction product by removing unincorporated dye terminators from a sequencing reaction of the claimed invention, as none of *Leonard* and *Bjerke*, alone or in combination, would have taught each and every limitation of the claimed invention. Additionally, Applicants respectfully contend that because *Bjerke* fails to teach or suggest using guanidine without any silica particles or silica magnetic particles to remove unincorporated dye terminators from the sequencing reaction products on a ultrafiltration membrane while applying a driving force to the ultrafiltration membrane, there is no reasonable expectation of success in modifying *Leonard* in view of *Bjerke* as alleged in the Office Action, even if *arguendo*, one of ordinary skill in the art would have been motivated to combine the teachings of *Leonard* with *Bjerke*.

Applicants respectfully contend that the PTO has not met its burden because neither *Leonard* nor *Bjerke*, either alone, or combined as alleged in the Office Action, teach or suggest all of the limitations contained in claim 1. Applicants respectfully contend that these remarks obviate the rejection of claims 2, 3 and 17 as well. Accordingly, Applicants respectfully contend that at least for these reasons, the *prima facie* case of obviousness has been rebutted and this rejection should be withdrawn.

2. Claims 1-3 and 16-20 were rejected under 35 USC 103(a), as being obvious over *Leonard* in view of *Bjerke*, and further in view of U.S. Patent No. 5,958,727 to *Brody et al.* (hereinafter referred to as "*Brody*") and U.S. Patent No. 5,202,456 to *Rando* (hereinafter referred to as "*Rando*").

The Office Action acknowledges that *Leonard* in view of *Bjerke* fail to teach using guanidine solution from 1mM to 60mM (claims 18-20), and fail to teach that the guanidine solution comprises EDTA (claim 16). However, the Office Action relies on *Brody* and *Rando* to overcome these deficiencies.

The PTO bears the burden of initially establishing a *prima facie* case of obviousness. Applicants respectfully contend that, as discussed *supra*, the PTO has not met its initial burden because neither *Leonard* nor *Bjerke*, either alone, or combined as alleged in the Office Action, teach or suggest all of the limitations contained in claim 1. Therefore, the Office Action's reliance on *Brody* and *Rando* fails to overcome the deficiencies *Leonard* and *Bjerke* as discussed *supra*. Additionally, since claims 2, 3 and 16-20 depend on claim 1, Applicants respectfully contend that these remarks obviate the rejection of these claims as well. Accordingly, Applicants respectfully contend that at least for these reasons, the *prima facie* case of obviousness has been rebutted and the rejection should be withdrawn.

IV. CONCLUSION

In view of the foregoing remarks, Applicants respectfully request the reconsideration and withdrawal of the rejections, and the timely allowance of the pending claims. Applicants believe that the above response is a complete response to the present office action. If however the Examiner believes that some requirement has been missed or not completely answered, the Examiner is invited to contact Applicants' attorney at the number below.

A petition for a three (3) months extension of time is being filed herewith. The Commissioner is hereby authorized to charge any deficiency in the fees or credit any overpayment to deposit account No. 133577, referencing Attorney Docket No. MCA-614US.

Respectfully submitted,

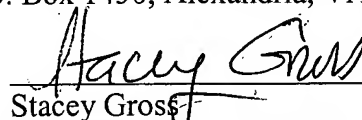


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March 11, 2008
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Stacey Gross